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L10: Entry 2 of 2

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May 1, 2003

DERWENT-ACC-NO: 2002-373930

DERWENT-WEEK: 200331

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TITLE: Identifying agents for treatment or prevention of cytomegalovirus infection, comprises contacting test compound with cellular kinase and detecting change in cellular kinase activity

INVENTOR: BEVEC, D; HABENBERGER, P ; [SCHUBART, D](#) ; STEIN-GERLACH, M

PRIORITY-DATA: 2000US-240750P (October 16, 2000), 2001US-0981397 (October 16, 2001)

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## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> <a href="#">US 20030082519 A1</a>	May 1, 2003		000	A61K039/395
<input type="checkbox"/> <a href="#">EP 1201765 A2</a>	May 2, 2002	E	049	C12Q001/48

INT-CL (IPC): [A01 N 61/00](#); [A61 K 31/00](#); [A61 K 39/395](#); [A61 K 48/00](#); [A61 P 31/12](#); [C07 K 16/00](#); [C12 P 21/06](#); [C12 Q 1/48](#); [C12 Q 1/68](#); [C12 Q 1/70](#); [G01 N 33/53](#)

ABSTRACTED-PUB-NO: EP 1201765A

## BASIC-ABSTRACT:

NOVELTY - Identifying compounds (A) for treating and/or preventing cytomegalovirus (CMV) infection and/or related diseases comprising contacting a test compound with at least one of the cellular kinases RICK, RIP, Nck-Interacting kinase, MKK3 and SRPK-2 (undefined) and detecting any change in kinase activity, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) detecting CMV infection and/or related diseases by detecting activity of any of the specified kinases in a patient sample, cells or cell lysates;
- (2) mono- or poly-clonal antibodies (Ab) that bind to any of the specified kinases;
- (3) preventing and/or treating CMV infection or related diseases, or for regulating production of CMV in an individual or cells, by administering an inhibitor or activator of any of the specified kinases;
- (4) oligonucleotides (ON) that bind to RNA or DNA encoding any of the specified kinases;
- (5) regulating expression of any of the specified kinases by administering to an

individual, or cells, an inhibitor or activator of transcription of the relevant DNA or translation of the relevant RNA;

(6) solid support for detecting CMV infection in an individual or cell comprising at least one immobilized ON able to detect activity of any of the specified kinases; and

(7) solid support for screening (A) comprising one or more immobilized ON that encode any of the specified kinases or these kinases themselves.

ACTIVITY - Virucide. RICK was transiently overexpressed, as a fusion with a hemagglutinin (HA) tag, in human embryonic kidney 293 cells, then immunoprecipitated (anti-HA antibody and protein A-Sepharose). The beads were washed, then tested for kinase activity by incubation in a mixture containing gamma (33P)-adenosine triphosphate and various concentrations of 8-methyl-6-phenyl-2-(pyridin-4-ylamino)-8H-pyrido(2,3-d)pyrimidin-7-one (Aa). After 30 minutes at 30 deg. C, reaction was stopped and phosphorylation determined by electrophoresis and autoradiography. (Aa) has an inhibitory concentration (IC)50 for inhibition of RICK of 500 nM and for inhibition of CMV of 1.4 micro M.

MECHANISM OF ACTION - Modulation of cellular kinases that are specifically upregulated during CMV infection.

USE - (A) are used to treat and/or prevent CMV infections and related diseases. Oligonucleotides that can detect the specified kinases can also be used for diagnosis of infection.

ABSTRACTED-PUB-NO: EP 1201765A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/2

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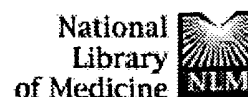
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		<i>DB=USPT; PLUR=YES; OP=ADJ</i>	
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<input type="checkbox"/>	L8	kinase RIP and CMV.clm.	1
<input type="checkbox"/>	L7	Rip kinase and CMV.clm.	0
<input type="checkbox"/>	L6	Rip kinases and CMV.clm.	0
<input type="checkbox"/>	L5	kinases and CMV.clm.	217
<input type="checkbox"/>	L4	kinases and CMV	5380
<input type="checkbox"/>	L3	L1 and virus	1
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☐ 1: [Yang Y, Ma J, Chen Y, Wu M.](#)[Related Articles, Links](#)

**Nucleocytoplasmic shuttling of RIP3: Identification of novel nuclear export and import signals in RIP3.**

J Biol Chem. 2004 Jun 18 [Epub ahead of print]

PMID: 15208320 [PubMed - as supplied by publisher]

☐ 2: [Hu WH, Mo XM, Walters WM, Brambilla R, Bethea JR.](#)[Related Articles, Links](#)

**TNAP, a novel repressor of NF-kappa B-inducing kinase, suppresses NF-kappa B activation.**

J Biol Chem. 2004 Jun 18 [Epub ahead of print]

PMID: 15208311 [PubMed - as supplied by publisher]

☐ 3: [Shen HM, Lin Y, Choksi S, Tran J, Jin T, Chang L, Karin M, Zhang J, Liu ZG.](#)[Related Articles, Links](#)

**Essential roles of receptor-interacting protein and TRAF2 in oxidative stress-induced cell death.**

Mol Cell Biol. 2004 Jul;24(13):5914-22.

PMID: 15199146 [PubMed - in process]

☐ 4: [Zha J, Zhou Q, Xu LG, Chen D, Li L, Zhai Z, Shu HB.](#)[Related Articles, Links](#)

**RIP5 is a RIP-homologous inducer of cell death.**

Biochem Biophys Res Commun. 2004 Jun 25;319(2):298-303.

PMID: 15178406 [PubMed - in process]

☐ 5: [Lee TH, Shank J, Cusson N, Kelliher MA.](#)[Related Articles, Links](#)

**The kinase activity of Rip 1 is not required for TNF-alpha-induced Ikk or p38 MAP kinase activation or for the ubiquitination of Rip 1 by Traf 2.**

J Biol Chem. 2004 Jun 1 [Epub ahead of print]

PMID: 15175328 [PubMed - as supplied by publisher]

☐ 6: [Kurenova E, Xu LH, Yang X, Baldwin AS Jr, Craven RJ, Hanks SK, Liu ZG, Cance WG.](#)[Related Articles, Links](#)

**Focal adhesion kinase suppresses apoptosis by binding to the death domain of receptor-interacting protein.**

Mol Cell Biol. 2004 May;24(10):4361-71.

PMID: 15121855 [PubMed - indexed for MEDLINE]

☐ 7: [Kilpatrick LE, Sun S, Korchak HM.](#)[Related Articles, Links](#)

**Selective Regulation by {delta}-PKC and PI 3-kinase in the Assembly of the Anti-Apoptotic TNFR-1 Signaling Complex in Neutrophils.**

Am J Physiol Cell Physiol. 2004 Apr 28 [Epub ahead of print]

PMID: 15115707 [PubMed - as supplied by publisher]

- ☐ **8:** [Meylan E, Burns K, Hofmann K, Blancheteau V, Martinon F, Kelliher M, Tschopp J.](#) [Related Articles, Links](#)
- ☐ **RIP1 is an essential mediator of Toll-like receptor 3-induced NF-kappa B activation.**  
Nat Immunol. 2004 May;5(5):503-7. Epub 2004 Apr 04.  
PMID: 15064760 [PubMed - indexed for MEDLINE]
- ☐ **9:** [Muller T, Langner C, Fuchsbichler A, Heinz-Erian P, Ellemunter H, Schlenck B, Bavdekar AR, Pradhan AM, Pandit A, Muller-Hocker J, Melter M, Kobayashi K, Nagasaka H, Kikuta H, Muller W, Tanner MS, Sternlieb I, Zatloukal K, Denk H.](#) [Related Articles, Links](#)
- ☐ **Immunohistochemical analysis of Mallory bodies in Wilsonian and non-Wilsonian hepatic copper toxicosis.**  
Hepatology. 2004 Apr;39(4):963-9.  
PMID: 15057900 [PubMed - indexed for MEDLINE]
- ☐ **10:** [Nho CW, O'Dwyer PJ.](#) [Related Articles, Links](#)
- ☐ **NF-kappaB activation by the chemopreventive dithiolethione oltipraz is exerted through stimulation of MEKK3 signaling.**  
J Biol Chem. 2004 Jun 18;279(25):26019-27. Epub 2004 Mar 26.  
PMID: 15047705 [PubMed - in process]
- ☐ **11:** [Omerovic J, Puggioni EM, Napoletano S, Visco V, Fraioli R, Frati L, Gulino A, Alimandi M.](#) [Related Articles, Links](#)
- ☐ **Ligand-regulated association of ErbB-4 to the transcriptional co-activator YAP65 controls transcription at the nuclear level.**  
Exp Cell Res. 2004 Apr 1;294(2):469-79.  
PMID: 15023535 [PubMed - indexed for MEDLINE]
- ☐ **12:** [Zhang HG, Wang J, Yang X, Hsu HC, Mountz JD.](#) [Related Articles, Links](#)
- ☐ **Regulation of apoptosis proteins in cancer cells by ubiquitin.**  
Oncogene. 2004 Mar 15;23(11):2009-15. Review.  
PMID: 15021888 [PubMed - indexed for MEDLINE]
- ☐ **13:** [Barcia RN, Valle NS, McLeod JD.](#) [Related Articles, Links](#)
- ☐ **Caspase involvement in RIP-associated CD95-induced T cell apoptosis.**  
Cell Immunol. 2003 Dec;226(2):78-85.  
PMID: 14962495 [PubMed - indexed for MEDLINE]
- ☐ **14:** [Huang J, Teng L, Li L, Liu T, Li L, Chen D, Xu LG, Zhai Z, Shu HB.](#) [Related Articles, Links](#)
- ☐ **ZNF216 Is an A20-like and IkappaB kinase gamma-interacting inhibitor of NFkappaB activation.**  
J Biol Chem. 2004 Apr 16;279(16):16847-53. Epub 2004 Jan 30.  
PMID: 14754897 [PubMed - in process]
- ☐ **15:** [Newton K, Sun X, Dixit VM.](#) [Related Articles, Links](#)
- ☐ **Kinase RIP3 is dispensable for normal NF-kappa Bs, signaling by the B-cell and T-cell receptors, tumor necrosis factor receptor 1, and Toll-like receptors 2 and 4.**  
Mol Cell Biol. 2004 Feb;24(4):1464-9.  
PMID: 14749364 [PubMed - indexed for MEDLINE]
- ☐ **16:** [Han KJ, Su X, Xu LG, Bin LH, Zhang J, Shu HB.](#) [Related Articles, Links](#)

Mechanisms of the TRIF-induced interferon-stimulated response element

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L8 ANSWER 1 OF 2 USPATFULL on STN  
AN 2004:63787 USPATFULL  
TI 14171 Protein kinase, a novel human protein kinase and uses thereof  
IN Kapeller-Libermann, Rosana, Chestnut Hill, MA, UNITED STATES  
PA Millennium Pharmaceuticals, Inc. (U.S. corporation)  
PI US 2004048305 A1 20040311  
AI US 2003-658904 A1 20030910 (10)  
RLI Continuation-in-part of Ser. No. US 2001-781882, filed on 12 Feb 2001,  
GRANTED, Pat. No. US 6630335  
PRAI US 2000-182096P 20000211 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 5414  
INCL INCLM: 435/006.000  
INCLS: 435/069.100; 435/194.000; 435/320.100; 435/325.000; 536/023.200  
NCL NCLM: 435/006.000  
NCLS: 435/069.100; 435/194.000; 435/320.100; 435/325.000; 536/023.200  
IC [7]  
ICM: C12Q001-68  
ICS: C07H021-04; C12N009-12  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 2 OF 2 USPATFULL on STN  
AN 2003:120036 USPATFULL  
TI Cellular kinases involved in **Cytomegalovirus** infection and  
their inhibition  
IN Schubart, Daniel, Weil am Rhein, GERMANY, FEDERAL REPUBLIC OF  
Habenberger, Peter, Munchen, GERMANY, FEDERAL REPUBLIC OF  
Stein-Gerlach, Matthias, Munchen, GERMANY, FEDERAL REPUBLIC OF  
Bevec, Dorian, Germering, GERMANY, FEDERAL REPUBLIC OF  
PI US 2003082519 A1 20030501  
AI US 2001-981397 A1 20011016 (9)  
PRAI US 2000-240750P 20001016 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 2300  
INCL INCLM: 435/005.000  
INCLS: 424/146.100; 514/001.000; 435/007.100; 435/069.100  
NCL NCLM: 435/005.000  
NCLS: 424/146.100; 514/001.000; 435/007.100; 435/069.100  
IC [7]  
ICM: A61K039-395  
ICS: C12Q001-70; A61K031-00; A01N061-00; G01N033-53; C12P021-06  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L2 18 S KINASE RIP  
L3 26525 S CYTOMEGALOVIRUS  
L4 0 S L2 AND L3  
L5 0 S L1 AND L3

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CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS,  
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L6 QUE RIP KINASE AND CYTOMEGALOVIRUS

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FILE 'CAPLUS' ENTERED AT 15:15:08 ON 06 JUL 2004

L7 1 S RIP KINASE AND CYTOMEGALOVIRUS

FILE 'USPATFULL' ENTERED AT 15:15:38 ON 06 JUL 2004

L8 2 S RIP KINASE AND CYTOMEGALOVIRUS